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(19) World Intellectual Property Organization  
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29 March 2001 (29.03.2001)

PCT

(10) International Publication Number  
**WO 01/21654 A3**

(51) International Patent Classification<sup>7</sup>: C12N 15/12, C07K 14/47, 16/18, G01N 33/50, 33/68

(21) International Application Number: PCT/US00/26338

(22) International Filing Date:  
25 September 2000 (25.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/404,967 24 September 1999 (24.09.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:  
US 09/404,967 (CIP)  
Filed on 23 September 1999 (23.09.1999)

(71) Applicant (for all designated States except US): RIGEL PHARMACEUTICALS, INC. [US/US]; 240 East Grand Avenue, South San Francisco, CA 94080 (US).

(71) Applicants and

(72) Inventors: LUO, Ying [CN/US]; 32 Chester Circle, Los Altos, CA 94022 (US). MANCEBO, Helena [CN/US]; Apartment 305, 4500 Susan Drive, San Bruno, CA 94066 (US).

(74) Agents: SILVA, Robin, M. et al.; Flehr Hohbach Test Albritton & Herbert LLP, Suite 3400, 4 Embarcadero Center, San Francisco, CA 94111-4187 (US).

(81) Designated States (national): AU, CA, JP, US.

(84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:

— with international search report

(88) Date of publication of the international search report:  
7 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SYK KINASE-ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE

MTVEQNVLQQSAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTA<sup>1</sup>KNAK  
TPQQEETTYQTALPGNDRYISVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET  
GITDEEQAIASRVLEASIAENKACLKRTPTEVWRDLSRNPyDRKRQDKAPVGLKNVGNTCW  
SAVIQSLFNLLEFRRRLVNYKPPSNAQDLPRNQKEERNLPMFRELRLYLALLVGTKRKYV  
DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPMVELFY  
GRFLAVGVLEGKKFENTEMFGQYPLQVNQFKDLHECLEAMIEGEIESLHSENSGKSGQE  
HWFTGLPPVLTFXLSRFEPNQALGRPEKIHNKLEFPQVLYLDRYMRHRNREITRIKREEIK  
RLKDYLTVLQQRLERYLSYGSGPKRFPPLVDLQYALEFASSKPVCSTPVDDIDASSPPSG  
SIPSQTLPSSTTEQQGALSSELPSTSVAISSLRSVIIHKPFTQSRIPPDLMHPAPRHI  
TEEELSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHE  
GQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCILMYINDK<sup>2</sup>AQ  
FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAQKALQEKLLASQ  
KLRESETSVTTAQAAQGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSA  
IKLEYARLVKLAQEDTPPETDYRLHHVVVFIQNQAPKKIEKTLLEQFGDRNL

(57) Abstract: The present invention is directed to polypeptides, nucleic acids and related molecules which have an effect on or are related to the cell cycle. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Further provided by the present invention are methods for identifying novel compositions which mediate cell cycle bioactivity, and the use of such compositions in diagnosis and treatment of disease.

WO 01/21654 A3

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/26338

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C12N15/12 C07K14/47 C07K16/18 G01N33/50 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 46289 A (HUMAN GENOME SCIENCES INC (US) RUBEN FERRIE ROSEN FLORENCE YOUNG YU NI) 16 September 1999 (1999-09-16) page 38, line 29 -page 41, line 6 page 105, line 34 -page 107, line 15; example 10 ----	1-18
E	WO 00 78934 A (SCHOOL OF PHARMACY LONDON UNIVERSITY (GB); NIZETIC DEAN; GROET JÜRGEN) 28 December 2000 (2000-12-28) SEQ ID NO:1 and 5 page 17, line 31 -page 21, line 18 page 30, line 28 -page 33, line 2 ----	1,2,4, 6-13, 15-23 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

16 July 2001

Date of mailing of the international search report

20/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Macchia, G

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/26338

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 79267 A (SCHOOL OF PHARMACY LONDON UNIVERSITY (GB); NIZETIC DEAN; GROET JÜRGEN) 28 December 2000 (2000-12-28) SEQ ID NO:1 and 5 abstract page 19, line 1 -page 21, line 21 ----	1,2,4, 6-13, 15-23
X	WO 94 25565 A (ARIAD PHARMA INC (US); BRUGGE MORGANSTERN SHIUE ZYDOWSKY ZOLLER PAWSON) 10 November 1994 (1994-11-10) page 21 -page 22; example 2 SEQ ID NO:1 page 34 -page 39 ----	15
X	WO 99 25829 A (CURAGEN CORP (US); YANG MEIJIA; NANDABALAN KRISHNAN; SCHULZ VINCENT P.) 27 May 1999 (1999-05-27) claims 47,58-62 ----	19-23
P,X	VALERO REBECA ET AL.: "USP25, a novel gene encoding a deubiquitinating enzyme, is located in the gene-poor region 21q11.2" GENOMICS, vol. 62, no. 3, 15 December 1999 (1999-12-15), pages 395-405, XP002153277 ISSN: 0888-7543 page 398 -page 399; figure 1 -----	1-5,7, 11-15

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15 in part

Present claim 15 relates to a polypeptide defined by reference to a desirable characteristic or property, namely its binding to the polypeptide(s) of present application.

The claim covers all polypeptides having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such polypeptides.

In fact, present application describes only the binding of the polypeptides disclosed to the SYK kinase (pages 4-5 and figure 7). Moreover on pages 43-48, present application refers to antibodies against the polypeptides of the invention. No other polypeptide having the above mentioned characteristic or property is defined in present application.

In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define a polypeptide by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the SYK kinase and to antibodies against the polypeptides of present application, as defined on pages 4-5 and 43-48 of present application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/26338

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9946289	A 16-09-1999	AU 3006799 A	27-09-1999		
		EP 1062236 A	27-12-2000		
		EP 1044210 A	18-10-2000		
		WO 9931116 A	24-06-1999		
WO 0078934	A 28-12-2000	AU 5550800 A	09-01-2001		
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		AU 5552400 A	09-01-2001		
		WO 0078934 A	28-12-2000		
WO 9425565	A 10-11-1994	CA 2160716 A	10-11-1994		
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		JP 8509380 T	08-10-1996		
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WO 9925829	A 27-05-1999	US 5986055 A	16-11-1999		
		AU 1522499 A	07-06-1999		
		EP 1030919 A	30-08-2000		

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(10) International Publication Number  
**WO 01/21654 A2**

(51) International Patent Classification<sup>7</sup>: C07K 14/00    (71) Applicants and

(21) International Application Number: PCT/US00/26338    (72) Inventors: LUO, Ying [CN/US]; 32 Chester Circle, Los Altos, CA 94022 (US). MANCEBO, Helena [CN/US]; Apartment 305, 4500 Susan Drive, San Bruno, CA 94066 (US).

(22) International Filing Date:  
25 September 2000 (25.09.2000)

(25) Filing Language: English    (74) Agents: SILVA, Robin, M. et al.; Flehr Hohbach Test Albritton & Herbert LLP, Suite 3400, 4 Embarcadero Center, San Francisco, CA 94111-4187 (US).

(26) Publication Language: English    (81) Designated States (*national*): AU, CA, JP, US.

(30) Priority Data:  
09/404,967    24 September 1999 (24.09.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:  
US                      09/404,967 (CIP)  
Filed on                23 September 1999 (23.09.1999)

(71) Applicant (*for all designated States except US*): RIGEL PHARMACEUTICALS, INC. [US/US]; 240 East Grand Avenue, South San Francisco, CA 94080 (US).

Published:

— *Without international search report and to be republished upon receipt of that report.*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: NOVEL SYK KINASE-ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE

MTVEQNLQQSAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTA<sup>1</sup>KNAK  
TPQQEETYYQTALPGNDRYISVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET  
GITDEEQAISRVLEASIAENKAICLKRTPTEVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF  
SAVIQSLFNLLFRRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV  
DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEEETDEEKPKNPVMVELFY  
GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAMIEGEIESLHSENSGKSGQE  
HWFTGLPPVLTFLXLSRFEFNQALGRPEKIHNKLEFPQVLYLDRYMHRNREITRIKREEIK  
RLKDYLTVLQQRLERYLSYSGSPKRFPLVDVLQYALEFASSKPVCSTPVDDIDASSPPSG  
SIPSQTLPSSTTEQQGALSSelpSTS PSSVAAISSRSVIHKPFTQSRIPPDLPMPAPRHI  
TEEEELSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHE  
GQANAGHYWAYIFDHRESRWMKYNDIAVTSSWEELVRDSFGGYRNASAYCLMYINDK<sup>2</sup>AQ  
FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEKELEEWDAQLAOKALQEKL LASQ  
KLRESETSVTTAQAAAGDPEYLEQPSRSDFSKHLKEETIQQITKASHEHEDKS PETVLOSA  
IKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQAPKKIEKTLLEQFGDRNL

WO 01/21654 A2

(57) Abstract: The present invention is directed to novel polypeptides, nucleic acids and related molecules which have an effect on or are related to the cell cycle. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Further provided by the present invention are methods for identifying novel compositions which mediate cell cycle bioactivity, and the use of such compositions in diagnosis and treatment of disease.

~~-File-~~

## PATENT COOPERATION TREATY

PCT

## NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

SILVA, Robin, M.  
 Flehr Hohbach Test Albritton &  
 Herbert LLP  
 Suite 3400  
 4 Embarcadero Center  
 San Francisco, CA 94111-4187  
 ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)  
 29 March 2001 (29.03.01)

Applicant's or agent's file reference  
 FP68412-1RMS ~~SD~~

## IMPORTANT NOTICE

International application No. PCT/US00/26338	International filing date (day/month/year) 25 September 2000 (25.09.00)	Priority date (day/month/year) 24 September 1999 (24.09.99)
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Applicant  
 RIGEL PHARMACEUTICALS, INC. et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
 AU,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
 CA,EP,JP

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on  
 29 March 2001 (29.03.01) under No. WO 01/21654

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>FP68412-1RMS</b>	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. <b>PCT/US 00/ 26338</b>	International filing date ( <i>day/month/year</i> ) <b>25/09/2000</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>24/09/1999</b>
Applicant <b>RIGEL PHARMACEUTICALS, INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**SYK KINASE-ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE**

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

**5**

- None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 15 in part

Present claim 15 relates to a polypeptide defined by reference to a desirable characteristic or property, namely its binding to the polypeptide(s) of present application.

The claim covers all polypeptides having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such polypeptides.

In fact, present application describes only the binding of the polypeptides disclosed to the SYK kinase (pages 4-5 and figure 7). Moreover on pages 43-48, present application refers to antibodies against the polypeptides of the invention. No other polypeptide having the above mentioned characteristic or property is defined in present application.

In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define a polypeptide by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the SYK kinase and to antibodies against the polypeptides of present application, as defined on pages 4-5 and 43-48 of present application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 00/26338

**Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)**

The present invention is directed to polypeptides, nucleic acids and related molecules which have an effect on or are related to the cell cycle. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention. Further provided by the present invention are methods for identifying novel compositions which mediate cell cycle bioactivity, and the use of such compositions in diagnosis and treatment of disease.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/26338

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9946289	A 16-09-1999	AU 3006799 A	EP 1062236 A	EP 1044210 A	27-09-1999 27-12-2000 18-10-2000
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WO 9925829	A 27-05-1999	US 5986055 A	AU 1522499 A	EP 1030919 A	16-11-1999 07-06-1999 30-08-2000

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/GB 00/02423

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0972837 A	19-01-2000	JP	11318471 A	24-11-1999
WO 9946289 A	16-09-1999	AU	3006799 A	27-09-1999
		EP	1044210 A	18-10-2000
		WO	9931116 A	24-06-1999

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/26338

A. CLASSIFICATION OF SUBJECT MATTER	IPC 7 C12N15/12 C07K14/47 C07K16/18 G01N33/50 G01N33/68
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According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

16 July 2001

Date of mailing of the international search report

20/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Macchia, G

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/26338

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 79267 A (SCHOOL OF PHARMACY LONDON UNIVERSITY (GB); NIZETIC DEAN; GROET JÜRGEN) 28 December 2000 (2000-12-28) SEQ ID NO:1 and 5 abstract page 19, line 1 -page 21, line 21 ---	1,2,4, 6-13, 15-23
X	WO 94 25565 A (ARIAD PHARMA INC (US); BRUGGE MORGANSTERN SHIUE ZYDOWSKY ZOLLER PAWSON) 10 November 1994 (1994-11-10) page 21 -page 22; example 2 SEQ ID NO:1 page 34 -page 39 ---	15
X	WO 99 25829 A (CURAGEN CORP (US); YANG MEIJIA; NANDABALAN KRISHNAN; SCHULZ VINCENT P.) 27 May 1999 (1999-05-27) claims 47,58-62 ---	19-23
P,X	VALERO REBECA ET AL.: "USP25, a novel gene encoding a deubiquitinating enzyme, is located in the gene-poor region 21q11.2" GENOMICS, vol. 62, no. 3, 15 December 1999 (1999-12-15), pages 395-405, XP002153277 ISSN: 0888-7543 page 398 -page 399; figure 1 -----	1-5,7, 11-15

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>9347.03/PC</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 01/ 02960</b>	International filing date (day/month/year) <b>14/03/2001</b>	(Earliest) Priority Date (day/month/year) <b>20/03/2000</b>
Applicant <b>SQUICCIARINI, Carlo</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable (See Box I).**

3.  **Unity of invention is lacking (see Box II).**

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

2

None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 01/ 02960

## Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

LINE 8: Insert "(16)" after after "columns"

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/02960

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 G01N1/00 G01N30/24 G01N1/34

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N B01D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 970 804 A (ROBBAT JR ALBERT) 26 October 1999 (1999-10-26) abstract column 3, line 41 -column 4, line 41; figure 8D ---	1-8,10
Y	EP 0 770 869 A (PERKIN ELMER CORP) 2 May 1997 (1997-05-02) column 5, line 26-30; figure 1 ---	1-8,10
Y	US 5 932 482 A (MARKELOV MICHAEL) 3 August 1999 (1999-08-03) column 7, line 55 -column 8, line 10; figure 3 abstract --- -/-	1-8,10



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

12 July 2001

Date of mailing of the international search report

20/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Brison, O

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/02960

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 191 211 A (GORMAN JR WILLIAM B) 2 March 1993 (1993-03-02) column 2, line 39 -column 3, line 20; figure 1 ---	1
A	US 5 690 828 A (JAMESON DANIEL GENE ET AL) 25 November 1997 (1997-11-25) abstract; figures 1-3 ---	1-10
A	US 5 588 988 A (GERSTEL EBERHARD ET AL) 31 December 1996 (1996-12-31) abstract; figure 1 ---	1
A	WO 96 27417 A (DIONEX CORP) 12 September 1996 (1996-09-12) abstract; figure 1 ---	1
A	US 5 065 614 A (BAKER CHRISTOPHER W ET AL) 19 November 1991 (1991-11-19) abstract -----	1

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 01/02960

Patent document cited in search report		Publication date		Patent family member(s)		Publication date	
US 5970804	A	26-10-1999		US 5668373 A AU 2817297 A AU 2925997 A CA 2252715 A EP 0895584 A WO 9741412 A WO 9741419 A		16-09-1997 19-11-1997 19-11-1997 06-11-1997 10-02-1999 06-11-1997 06-11-1997	
EP 0770869	A	02-05-1997		JP 9133668 A US 5711786 A		20-05-1997 27-01-1998	
US 5932482	A	03-08-1999		NONE			
US 5191211	A	02-03-1993		NONE			
US 5690828	A	25-11-1997		US 5268102 A US 5198197 A US 5160624 A US 5094753 A US 6241890 B US 5911881 A DE 69412393 D DE 69412393 T EP 0639099 A JP 8506997 T WO 9420190 A US 5269930 A US 5268103 A US 6149814 A US 6071408 A US 5584989 A US 5635070 A US 5601707 A US 5614089 A US 5653885 A US 5755559 A US 5738498 A US 5750027 A US 6086767 A US 6083399 A DE 69228979 D DE 69228979 T EP 0543471 A JP 5220302 A US 5296145 A US 6251267 B US 5932095 A US 5173188 A US 5250195 A DE 69118032 D DE 69118032 T EP 0466291 A EP 0665044 A JP 6058415 A US 5132014 A		07-12-1993 30-03-1993 03-11-1992 10-03-1992 05-06-2001 15-06-1999 17-09-1998 24-12-1998 22-02-1995 30-07-1996 15-09-1994 14-12-1993 07-12-1993 21-11-2000 06-06-2000 17-12-1996 03-06-1997 11-02-1997 25-03-1997 05-08-1997 26-05-1998 14-04-1998 12-05-1998 11-07-2000 04-07-2000 27-05-1999 19-08-1999 26-05-1993 31-08-1993 22-03-1994 26-06-2001 03-08-1999 22-12-1992 05-10-1993 25-04-1996 01-08-1996 15-01-1992 02-08-1995 01-03-1994 21-07-1992	
US 5588988	A	31-12-1996		DE 4419596 C		01-06-1995	

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/EP 01/02960

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9627417	A 12-09-1996	US 5660727 A		26-08-1997
		AU 695104 B		06-08-1998
		AU 5181596 A		23-09-1996
		CA 2214526 A		12-09-1996
		EP 0820334 A		28-01-1998
		JP 11501567 T		09-02-1999
		US 5785856 A		28-07-1998
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US 5065614	A 19-11-1991	DE 4191754 T		08-10-1992
		GB 2253161 A,B		02-09-1992
		WO 9202813 A		20-02-1992
		US 5123276 A		23-06-1992
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PCT

WIPO PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FP68412-1RMS	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/26338	International filing date (day/month/year) 25/09/2000	Priority date (day/month/year) 24/09/1999	
International Patent Classification (IPC) or national classification and IPC C07K14/00			
Applicant RIGEL PHARMACEUTICALS, INC. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand 20/04/2001	Date of completion of this report 08.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giebel, K Telephone No. +49 89 2399 8546



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/26338

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-51 as originally filed

**Claims, No.:**

1-23 as originally filed

**Drawings, sheets:**

1/8-8/8 as originally filed

**Sequence listing part of the description, pages:**

1-17, filed with the letter of 06.04.01

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/26338

the description, pages:

the claims, Nos.:

the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.

claims Nos. 1,2,18-23 (all completely), 6-11,15 (all partially).

because:

the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1,2,18-23 (all completely), 6-11 (all partially) are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**

the claims, or said claims Nos. 1,2,18-23 (all completely), 6-11 (all partially) are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. 15 (partially).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/26338

**1. Statement**

Novelty (N)	Yes:	Claims 3,5,14
	No:	Claims 4,6-13,15-17
Inventive step (IS)	Yes:	Claims
	No:	Claims 3,5,14
Industrial applicability (IA)	Yes:	Claims 3-17
	No:	Claims

**2. Citations and explanations**  
**see separate sheet**

**VI. Certain documents cited**

**1. Certain published documents (Rule 70.10)**

and / or

**2. Non-written disclosures (Rule 70.9)**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/26338

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. No meaningful opinion could be formed on claims 1, 2, 18-23 (all completely) and claims 6-11 (all partially) since these claims lack clarity and support by the description.

The term "cell cycle protein" used throughout the claims is vague and unclear in the context of the present application. It is not clear which activity the protein should have and which test should be employed to determine this activity. It is thus impossible for the skilled reader to determine without undue burden of experimentation whether or not a given protein is encompassed by said term. A meaningful opinion could only be formed on those claims which define the nucleic acids or proteins in question by clear technical features.

Claim 18 is completely unclear since "the biological function" of "said cell cycle protein" is not disclosed in the application. Claim 1 referring to hybridization is also not considered to be clear, firstly since the nature of the hybridization conditions depends on the circumstances, and secondly since the claim encompasses short portions or fragments (see the description, pages 8-9).

Consequently, only claims 3-5, 12-14, 16 and 17 (all completely) and claims 6-11 when referring back to these claims have been subject to examination.

The claims furthermore lack support by the description since the application does not demonstrate that the protein having the amino acid sequence of Figure 2 or 4 plays a role in the cell cycle.

Claim 14 could only be examined to the extend to which it has been searched (see the International Search Report).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/26338

2. The following documents are cited:

D1: WO 99 46289 A

D4: WO 94 25565 A

D6: GENOMICS, vol. 62, no. 3, 15 December 1999, pages 395-405

3. The current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document D6 cited in the international search report would become relevant.
4. The present application does not satisfy the criterion set forth in Article 33(1)(2) PCT because the subject-matter of claims 4, 6-13 and 15-17 is not new.

The document D1 discloses a polypeptide having the amino acid sequence of SEQ ID NO:130 which is 99% identical to SEQ ID NO:3 of the present application. Also disclosed are DNAs encoding said protein, vectors and antibodies.

The document is thus prejudicial to the novelty of claims 4, 6-13 and 15-17.

Claim 15 also lacks novelty over D4 which discloses the SYK protein.

The cells of claim 7 furthermore lack novelty since they are not clearly distinguished over known mammalian cells. The term "recombinant" is not suitable to distinguish the claimed cells over the prior art.

5. Claims 3, 5 and 14 relating to nucleic acids/polypeptides having the specific sequences disclosed in the present application are considered to lack an inventive step, since it would have been obvious to obtain these sequences in view of D1. Moreover, the application provides no **evidence** of the biological role of the disclosed polypeptide. Consequently, the invention of the present application is considered merely to be the provision of a transcribed sequence ("a DNA") with no known technical useful property. In this case, **any** prior art compound (e.g. DNA or protein) is equally suitable as the starting point for making structural modifications and may be considered as the "closest prior art". Starting from this point, the only technical problem which may be derived is the provision of a further compound as such, regardless of its useful properties. Without the concomitant need to provide any particular technical effect, the skilled

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/26338

person would have had the choice of an infinite number of equally possible solutions. An arbitrary selection from this host of possible solutions cannot involve an inventive step because, in order to be inventive, the selection must not be arbitrary but must be justified by the technical purpose, i.e. by a hitherto unknown or unexpected technical effect which is caused by those structural features distinguishing the claimed compound from the numerous other ones. Therefore, no inventive step can be acknowledged.

**Re Item VI**

**Certain documents cited**

6. Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 00/78934	28.12.00	22.06.00	22.06.99 03.04.00
WO 00/79267	28.12.00	22.06.00	22.06.99 03.04.00

**Re Item VIII**

**Certain observations on the international application**

7. The application does not meet the requirements of Article 6 PCT because the claims do not clearly define the matter form which protection is sought, see point 1 above.

Moreover, the requirements of Articles 5 and 6 PCT are not fulfilled since the scope of the claims is not justified by the technical contribution which the application makes over the prior art.